Q&A column

Q. I read your response concerning anticoagulant adjustment for hematocrits greater than 55 percent (CAP TODAY Q&A column, August 2016). Is it necessary to correct for hematocrits less than 20 percent?

A. Most literature and laboratory practice guidelines address adjustment of the volume of 3.2 percent citrate in the standard whole blood collection tube to ensure adequate sodium citrate concentration in a plasma sample when a patient's hematocrit is greater than 55 percent. The formula is: $C = 1.85 \times 10^{-3} \times (100 - Hct) \times V$. C stands for the volume (mL) of citrate in the standard blood collection tube, Hct is the hematocrit (%) of the patient, and V (mL) is the final volume of the whole blood sample. When the Hct is low, the final citrate concentration in a plasma sample is presumably lower than the optimal level for clotting time testing, which could result in a shortening of clotting times. In principle, the aforementioned formula can still be used when the Hct is lower than 20 percent. In a standard 3-mL citrate tube, a total of 0.44 mL citrate solution should be present in the tube, which means an additional 0.14 mL of citrate solution needs to be added to the existing 0.3 mL citrate solution in the tube. Given the rarity of this situation and a lack of validation studies in the literature, no coagulation laboratory guidelines recommend this adjustment. Thus, I would not recommend adjusting the citrate level in the tube when a patient's Hct is less than 20 percent. Instead, I would recommend measuring factor activities or anticoagulant levels by specific assays depending on various clinical questions since most of these assays require significant dilution of the patient's plasma, which makes the inadequately low citrate concentration in a plasma sample negligible.

Dong Chen, MD, PhD, Special Coagulation Laboratory, Mayo Clinic, Rochester, Minn.
Chair, CAP Coagulation Resource Committee

Q. What is the substitute test for HbA_{1c} for a patient with homozygous variant hemoglobin? Is a fructosamine and/or glycated albumin test appropriate?

A. Measurement of the concentration of glucose in the blood reveals an individual's glycemia at the time of phlebotomy. By contrast, hemoglobin A_{1c} concentration is a marker of chronic glycemia and indicates the average blood glucose concentration over approximately eight to 12 weeks. HbA_{1c} is formed by the nonenzymatic attachment of glucose to the N-terminal valine of the beta chain of HbA. Certain homozygous variant hemoglobins lack the N-terminal valine on the beta chain and therefore are unable to form HbA_{1c}. In addition, some variant hemoglobins alter red blood cell lifespan. If red cell lifespan is shortened, there is less time for HbA_{1c} to form and concentrations in the blood are lower than expected from the average glycemia.

Nonenzymatic attachment of glucose to other proteins to form ketoamines also occurs in the blood. Fructosamine is the generic name for all plasma protein ketoamines. Albumin is the most abundant serum protein and constitutes approximately 65 percent of total serum protein. The half-life of albumin in the circulation is 14–20 days, so the concentration of fructosamine or glycated albumin in the blood indicates average glucose concentration over the preceding two to three weeks. Automated, commercial assays are available to measure fructosamine or glycated albumin in the blood. These assays can be used as a measure of chronic glycemia in those situations where HbA_{1c} does not accurately reflect average glycemia.

There are some considerations that need to be borne in mind when interpreting fructosamine or glycated albumin results. Values can be altered independently of glycemia, particularly when albumin concentrations are changed. Examples include cirrhosis, nephrotic syndrome, and hyperuricemia. Conditions that alter serum protein concentrations include liver disease, thyroid disease, and renal disease. In addition, both assays are limited by the absence of strong evidence linking them to clinical outcomes in patients, particularly the long-term complications of diabetes. Therefore, there are no accepted thresholds for diagnosis of diabetes or goals for therapy in diabetes.

Additional clinical studies are required to yield further insight into the clinical roles of fructosamine and glycated albumin in patients with diabetes.

Welsh KJ, Kirkman MS, Sacks DB. Role of glycated proteins in the diagnosis and management of diabetes: research gaps and future directions. *Diabetes Care.* 2016;39(8):1299–1306.

David B. Sacks, MB ChB, Chief of Clinical Chemistry, Department of Laboratory Medicine,
National Institutes of Health Clinical Center, Bethesda, Md.
Member, CAP Chemistry Resource Committee